REMARKS

Claims 25 and 26 have been amended to reflect that the monoclonal antibodies produced bind specifically to gamma-carboxylated osteocalcin fragments of SEQ. ID NO. 2. Claim 25 has also been made definite by claiming that the antibodies "bind" instead of "are capable of binding" to said fragments. Claims 25 and 26 have been amended to indicate that the fragments are comprised of amino acids from position 7 to 30 or 6 to 30, respectively, of SEQ. ID NO. 2, both with gamma-carboxylated glutamic acids at position 17, 21 and 24. It is submitted that these amendments are made solely to clarify the language of the claims and do not narrow the scope of the claims. Finally, claim 26 has been amended to include additional steps needed to perform a non-competitive immunoassay. It is submitted that these amendments do not constitute new matter, and their entry is requested.

The Examiner objected to claims 5, 8, 25, and 26 because the dependent claims do not reference a previous claim. It is customary practice within the Patent Office to renumber the claims after allowance. In view of the accepted practice not to rewrite all of the claims in response to an Office Action, it is believed that it is unnecessary to make any changes to the claims at this point in response to the objection.

The Examiner rejected claims 5, 8, 25 and 26 under the second paragraph of 35 U.S.C. § 112 as being indefinite. Claims 25 and 26 have been amended to indicate that the monoclonal antibodies bind to an osteocalcin fragment which comprises either amino acids 7 to 30, or amino acids 6 to 30 of SEQ ID NO:2, wherein both fragments contain three gamma-carboxylated glutamic acids at positions 17, 21 and 24. The objectionable ambiguous language has been removed from claim 25, and it now clearly states that the monoclonal antibody binds human-carboxylated osteocalcin fragments. Additionally, claim 26 has been amended to include all necessary steps for the non-competitive immunoassay. Detection and correlation steps have been added to those previously listed. However, it is submitted that a separation step is not necessary for all immunoassays, such as a homogenous assay, as is well known in the art. The inclusion of the additional steps should provide the desired specificity, with the goal that duplication by one skilled in the art may be

accomplished. It is submitted that these amendments obviate the 35 U.S.C. § 112, second paragraph rejection, and its withdrawal is requested.

The Examiner also rejected claims 5, 8, 25 and 26 under 35 U.S.C. § 112, first paragraph, as failing to provide sufficiently detailed description so as to convey to one skilled in the art that the inventor(s) had possession of the claimed invention. It is urged, however, that the claims provide a sufficiently detailed description. Five monoclonal antibodies, 2H9, 6F9, 3G8, IC4, and 3H8, are set forth and are species of a genus. It may be argued that only these five monoclonal antibodies may be envisioned, because only these five monoclonal antibodies were specifically described. This argument may be countered, however, with the showing that said five monoclonal antibodies are precisely the sort of information that imparts information to one skilled in the art that Applicants are in possession of the genus. First, monoclonal antibodies have a well-documented, and highly specific, structure. Second, the binding site of the monoclonal antibodies is equally defined by the epitope to which it binds, specifically gamma-carboxylate osteocalcin fragments comprising specified amino acids of SEQ ID NO:2 in the instant case. Therefore, the invention properly defines a highly structured molecule, a monoclonal antibody, which binds to a particular target, gamma-carboxylated osteocalcin fragments of SEQ ID NO:2, as set forth in the claims.

The Examiner also contends that a generic statement which defines a genus by its functional activity is inadequate written description of the genus. As described, however, the specification and claims do not set forth a generic statement which is limited to functional activity. Instead, the specification describes a genus of molecules, i.e. monoclonal antibodies, the structure of which is well-known to one skilled in the art, that bind to specific gamma-carboxylated osteocalcin fragments of SEQ ID NO:2. The specification illustrates the genus by describing the production of five monoclonal antibodies which have this binding specificity. The Examiner contends that the production of one of the five specified monoclonal antibodies is not possible without undue experimentation. However, when one considers that the specification sets forth said five monoclonal antibodies as species of the genus, the Examiner's contention is traversed, because other monoclonal antibodies that bind to fragments of SEQ. ID NO:2 may be created, as set forth in the invention. The

five monoclonal antibodies created and described in the specification are species of the genus of monoclonal antibodies that bind to fragments of SEQ ID NO:2.

The Examiner's attention is directed to the recent case *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 62 U.S.P.Q.2d 1289 (Fed. Cir. 2002). In *Enzo*, the claims were directed to a nucleic acid probe and Enzo argued that there was written description on the basis of binding affinity citing to the Written Description Guidelines. Enzo pointed to the statement that, "'For some biomolecules, examples of identifying characteristics include a sequence, structure, binding affinity, binding specificity, molecular weight, and length.'" 62 U.S.P.Q.2d (BNA) at 1293. (quoting Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, 66 Fed. Reg. 1,099, 1110 (Jan. 5, 2001) ("Guidelines")). The Federal Circuit, however, found that Enzo's claims were insufficient. *Id.* The court found that a description may fulfill the requirement set forth in 35 U.S.C. § 112, first paragraph, if an applicant describes an invention by disclosing "'functional characteristics when coupled with a known or disclosed correlation between function and structure.'" Id. (quoting Guidelines, 66 Fed. Reg. 1,099, 1106 (Jan. 5, 2001)). The court stated that, "'[A]n isolated antibody capable of binding to antigen X,' considering 'the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature,'" is sufficient to satisfy 35 U.S.C. § 112, first paragraph. *Id.* (quoting Synopsis of Application of Written Description Guidelines, at 60, available at http://www.uspto.gov/web/patents/guides.htm). Thus, the Federal Circuit has concurred with the Written Description Guidelines that a monoclonal antibody binding to a specific antigen has sufficient structural characteristics to meet the written description requirements of 35 U.S.C. § 112, first paragraph.

As held by the Federal Circuit, a description of a DNA probe's binding affinity does not allow one skilled in the art to visualize the structure or other identifying characteristic that would differentiate it from similar probes. A monoclonal antibody, however, has a known structure and the existence of a specific epitope that binds to a highly particular target is sufficiently descriptive to allow one skilled in the art to visualize both its structure and function. It is therefore submitted

that the rejection under 35 U.S.C § 112, first paragraph for inadequate written description, is in error, and it is requested that the rejection be withdrawn.

Claims 5, 8, 25, and 26 were also objected to under 35 U.S.C. § 112, first paragraph, for failure to enable one skilled in the art because of incomplete deposit information. It is submitted that deposit of the monoclonal antibodies described in the specification is not required. First, the present specification's disclosure of five monoclonal antibodies demonstrates that monoclonal antibodies specific for the gamma-carboxylated osteocalcin fragments are routinely produced and identified by screening. The specification clearly demonstrates that undue experimentation is not required to produce additional monoclonal antibodies to the specified epitopes. Second, the facts of the present application are similar to those in *In re Wands*, 858 F.2d 731, 736 (Fed. Cir. 1988). In *Wands*, the Court found that so long as the specification fully enables the claimed invention, there is no need for the deposit of living cells. Moreover, the court held that enablement is not precluded by some experimentation, including routine screening. *Id.* at 737 (citations omitted). Specifically, the court held that a description of the production of several species of the claimed genus of monoclonal antibodies enabled the production and screening of monoclonal antibodies to identify additional monoclonal antibodies by a person of ordinary skill in the art without undue experimentation. If the skill in the art at the time of the Wands application was such that the Wands application was enabling, it is submitted that the present application, filed more than ten years later, is no less enabling for the claimed genus. The present specification describes the preparation of the claimed monoclonal antibodies with the same specificity and detail as in *Wands*. In fact, if the Examiner believes that the present claims are not enabled, she is invited to apply the *Wands* factors as required. Therefore, it is submitted that the production of a monoclonal antibody that binds to fragments of SEQ. ID NO:2 does not require undue experimentation.

Third, and furthermore, the present claims are not claiming the specific monoclonal antibodies 2H9, 6F9, 3G8, 1C4 and 3H8. It is therefore submitted that deposit of said five monoclonal antibodies specified is unnecessary, and it is requested that the rejection be withdrawn.

In view of the above amendments and remarks, it is believed that the claims satisfy the requirements of the patent statutes and are patentable over the prior art. Reconsideration of the instant application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

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Attachments: Marked-up Copy of Amended Claims

Marked-Up Copy of the Amended Claims

25 (amended). A monoclonal antibody or recombinant antibody fragment [having the capability of binding] which binds a human gamma-carboxylated osteocalcin fragment, said monoclonal antibody or recombinant antibody fragment has the specificity to epitopes that have been identified on said gamma-carboxylated fragment of osteocalcin, said osteocalcin fragment selected from the group consisting of

i) a fragment which [spans from amino acid in position 7 to amino acid in position 30] comprises amino acids 7-30 of the amino acid sequence set forth in SEQ ID NO:2 in which all three glutamic acids in positions 17, 21 and 24 of said sequence are gamma-carboxylated, and

ii) a fragment which [spans from amino acid in position 6 to amino acid in position 30] comprises amino acids 6-30 of the amino acid sequence of SEQ ID NO:2[, and that] in which all three glutamic acids in the positions 17, 21 and 24 of said sequence are gamma-carboxylated.

26 (amended). A non-competitive immunoassay for quantitative determination of a gamma-carboxylated osteocalcin fragment comprising contacting a sample containing said osteocalcin fragment with two monoclonal antibodies or recombinant antibody fragments which bind said osteocalcin fragment, [and] detecting bound monoclonal antibody or recombinant antibody fragment and correlating bound monoclonal antibody or recombinant antibody fragments with amount of osteocalcin present, wherein said monoclonal antibody or recombinant antibody fragment has the specificity to epitopes that have been identified on said gamma-carboxylated fragment of osteocalcin, said osteocalcin fragment selected from the group consisting of having consisting of

i) a fragment which [spans from] amino acid in position 7 to amino acid in position 30] comprises amino acids 7-30 of the amino acid sequence set forth in SEQ ID NO:2 in which all three glutamic acids in positions 17, 21 and 24 of said sequence are gamma-carboxylated, and

including

ii) a fragment which [spans from amino acid in position 6 to amino acid in position 30] comprises amino acids 6-30 of the amino acid sequence of SEQ ID NO:2[, and that] in which all three glutamic acids in the positions 17, 21 and 24 of said sequence are gamma-carboxylated.